Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Multiple SARS-CoV-2 Reinfections: A Case Series of Thrice-Infected Individuals

To the Editor: More than 1 in 4 individuals in the United States have now experienced a COVID-19 (coronavirus disease 2019) infection. Symptomatic reinfection despite positive serology has been documented,[1,2] but little is known about the impact of reinfection on subsequent natural immunity. In a study conducted prior to the omicron variant's prevalence, vaccination added no additional protection to natural immunity in the first year; however, booster impact was not ascertained.[3] In a cohort of health care professionals (HCPs), vaccination in previously infected individuals was associated with lower risk of reinfection over time.[4] Some have argued that HCPs with prior infection should be exempt from vaccine mandates indefinitely.[5]

We identified 11 HCPs with a distinct third infection (Table). Cases were captured via a robust program to identify and evaluate infected HCPs as previously described.[6] All HCPs were employed by a large health care institution with sites in 4 states employing over 73,000 HCPs. The study was deemed exempt by the Mayo Clinic Institutional Review Board (20-003887). Infections were classified as a repeat infection if occurring more than 90 days after a prior infection or if new COVID-19 symptoms began after complete resolution of prior symptoms. The 2 individuals reinfected within 90 days reported new anosmia. The median age was 27 years (range, 22 to 56 years), and 10 of the 11 HCPs were female. Of the first infections, 90.9% (10 of 11) occurred before the emergence of variants; 63.6% of second infections (7 of 11) occurred during delta variant predominance, and 90.9% of third infections (10 of 11) occurred during omicron prevalence. Vaccination status at the time of the 33 infections was unvaccinated in 20 (60.6%), booster overdue in 8 (24.2%), up to date in 4 (12.1%), or partially vaccinated in 1 (3.0%). Among the 11

TABLE 1. Characteristics of SARS-CoV-2 Reinfections[a]

Age/sex, state	Infection dates,[b] test method, locally predominant variant,[c] vaccination status,[d] symptom status, other test reason[e]			Days between 1st and 2nd infection	Days between 2nd and 3rd infection
26/F, Florida	3/26/2020 PCR NA Unvaccinated Symptomatic Occupational exposure	8/2/2021 PCR ≥85% Delta Unvaccinated Symptomatic Household exposure	1/21/2022 PCR ≥85% Omicron Unvaccinated Asymptomatic Surveillance	494	172
23/F, Wisconsin	9/7/2020 PCR NA Unvaccinated Symptomatic Community exposure	12/19/2021 PCR Mixed delta and omicron Booster overdue Symptomatic	1/29/2022 PCR ≥85% Omicron Booster Overdue Symptomatic	468	41
32/F, Wisconsin	10/19/2020 PCR NA Unvaccinated Symptomatic Household exposure	10/16/2021 PCR ≥85% Delta Booster overdue Symptomatic Household exposure	1/24/2022 Antigen (Flowflex) ≥85% Omicron Booster overdue Symptomatic Community exposure	362	100
25/F, Minnesota	10/25/2020 PCR NA Unvaccinated Symptomatic	9/24/2021 PCR ≥85% Delta Unvaccinated Asymptomatic Community exposure	1/19/2022 PCR ≥85% Omicron Unvaccinated Asymptomatic Surveillance	334	117

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TABLE 1. Continued

Age/sex, state	Infection dates,[b] test method, locally predominant variant,[c] vaccination status,[d] symptom status, other test reason[e]			Days between 1st and 2nd infection	Days between 2nd and 3rd infection
32/F, Minnesota	11/5/2020 PCR NA Unvaccinated Symptomatic	10/4/2021 PCR ≥85% Delta Booster overdue Asymptomatic Household exposure	1/3/2022 PCR Mixed delta/omicron Booster overdue Symptomatic	333	91
43/M, Minnesota	11/5/2020 PCR NA Unvaccinated Symptomatic	6/30/2021 PCR ≥85% Alpha Partially vaccinated Symptomatic	1/25/2022 PCR ≥85% Omicron Booster overdue Asymptomatic	237	209
27/F, Minnesota	11/7/2020 PCR NA Unvaccinated Symptomatic	10/21/2021 Antigen (On/Go) ≥85% Delta Unvaccinated Symptomatic Household exposure	1/22/22 PCR ≥85% Omicron Unvaccinated Asymptomatic Surveillance	348	93
25/F, Wisconsin	11/28/2020 PCR NA Unvaccinated Symptomatic	8/9/2021 PCR ≥85% Delta Booster overdue Symptomatic Posttravel	1/16/2022 PCR ≥85% Omicron Up to date Symptomatic Household exposure	254	160
46/F, Minnesota	12/17/2020 PCR NA Unvaccinated Symptomatic	4/5/2021 PCR ≥85% Alpha Up to date Asymptomatic Pretravel	1/22/2022 PCR ≥85% Omicron Up to date Symptomatic	109	292
56/F, Minnesota	1/30/2021 PCR NA Unvaccinated Asymptomatic Surveillance	12/23/2021 PCR Mixed delta and omicron Unvaccinated Asymptomatic Surveillance	1/22/2022 PCR ≥85% Omicron Unvaccinated Symptomatic	327	30
22/F, Minnesota	3/2/2021 PCR ≥85% Alpha Unvaccinated Asymptomatic Surveillance	9/7/2021 PCR ≥85% Delta Unvaccinated Symptomatic	1/27/2022 PCR ≥85% Omicron Up to date Asymptomatic Surveillance	189	142

[a]F, female; M, male; mRNA, messenger RNA; NA, not applicable; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[b]Infection date is date of symptom onset or date of positive test result if asymptomatic.

[c]Predominant circulating strain at the time of the infection in the individual's state per nextstrain.org. If a single variant accounted for ≥85% of sequenced infections, that variant is listed alone. If no variant accounted for 85% of infections, all circulating strains identified at that time in that state are listed.

[d]Vaccination status is "unvaccinated" when no doses have been received, "partially vaccinated" when one dose of mRNA vaccine has been received or a primary vaccination series was completed in the prior 14 days, "up to date" when a booster dose has been received or is not yet due (primary vaccination with mRNA vaccine was completed within the prior 5 months or Janssen vaccine within the prior 2 months), and "booster overdue" when primary vaccination with mRNA vaccine was completed more than 5 months earlier or Janssen vaccine more than 2 months earlier.

[e]Postexposure tests were performed within 14 days of prolonged close contact with a communicable source without recommended personal protective equipment. Surveillance testing programs were in place starting September 2, 2020, for workers in long-term care facilities and January 17, 2022, for unvaccinated staff.

HCPs, first, second, and third infections were asymptomatic in 2 (18.2%), 4 (36.4%), and 5 (45.4%), respectively. One second infection required hospitalization; no HCPs endorsed immunosuppression. The mean time to second infection was 314 days (95% CI, 238 to 390 days), while the mean interval between the second and third infection was 110 days (95% CI, 81 to 183 days) (P=.008 for difference in means).

This case series is subject to limitations. Following current public health guidance, postinfection testing to document polymerase chain reaction clearance was not routinely performed. However, persistence of polymerase chain reaction positivity longer than 90 days in immunocompetent individuals is unusual. Second, most third infections occurred during the omicron surge, and other variants may not display the same immune evasion to natural immunity. Third, the number of infections is too small to draw conclusions about the protective effect of prior infection or vaccination. Finally, samples were not available for genetic sequencing to confirm the variant(s) causing infection.

This case series provides new evidence of the potential for multiple reinfections in immunocompetent individuals. We noted a shorter interval between the second and third infections compared with the interval between the first and second infections, recognizing that almost all third infections occurred while the omicron variant was the predominant circulating strain. Omicron is known to partially evade vaccine-mediated and natural immunity.[7] Although infection and vaccination appear to impart short-term protection of a similar magnitude,[8] vaccination may still boost immunity or provide protection against new variants in individuals with one or more natural infections.

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Impact of the COVID-19 Pandemic on Respiratory Infection Rates

To the Editor: A substantial change in the pattern of influenza infections was noted worldwide[1] during the COVID-19 pandemic. We sought to describe our experience with seasonal respiratory infections across 60 sites of a major health care system in the Midwest United States. Although timing varies slightly from year to year, seasonal acute respiratory infections, such as influenza A/B, respiratory syncytial virus (RSV), and group A streptococcus (GAS), have predictable months of increased activity. We collected the number of tests performed for influenza A/B, RSV, GAS, and SARS-CoV-2 from November 1, 2018, to March 31, 2020 (ie, the pre-pandemic period) and April 1, 2020, to June 24, 2021 (ie, the pandemic period). During the COVID-19 pandemic, we observed lower rates of influenza A/B than previously reported and discovered substantially decreased positivity rates for RSV and GAS as well.[1-4]

A total of 1,489,293 tests were performed for influenza A/B, RSV, GAS, and SARS-CoV-2 between November 1, 2018, and June 24, 2021 (Table; Supplemental Figure, available online at http://www.